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Predictive Model of Diagnosing Probable Cases of Severe Acute Respiratory Syndrome in Febrile Patients With Exposure Risk

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Study objective: Since the World Health Organization issued a global alert about severe acute respiratory syndrome (SARS) on March 12, 2003, the illness has become a major public health challenge worldwide. The objective of this study is to identify the clinical risk factors of SARS and to develop a scoring system for early diagnosis.

Methods: The detailed clinical data of all patients presenting to the emergency department (ED) with a temperature higher than 38.0°C (100.3°F), documented at home or at the ED, and risks of exposure to SARS within 14 days were assessed. The diagnosis of probable SARS was made according to the definition of the Centers for Disease Control and Prevention. Items with significant differences among symptoms, signs, and laboratory tests on presentation between SARS and non-SARS groups were determined and used to develop the scoring system.

Results: Seventy patients were enrolled and 8 were diagnosed as probably having SARS. None of the initially discharged patients or their relatives developed SARS. Compared with the non-SARS group, the SARS group was younger (33.9±15.9 years versus 44±9.8 years; P=.02), had a higher percentage of fever prolonged more than 5 days (87.5% versus 6.5%; P<.01), myalgia (75% versus 27.4%; P=.01), and diarrhea (50% versus 9.7%; P=.02); had less occurrence of cough before or during fever (0% versus 64.5%; P=.01); and had lower absolute lymphocyte ($0.9\pm0.3\times10^9$/L versus $1.5\pm1.1\times10^9$/L; P<.01) and platelet counts ($144.1\pm36.3\times10^9$/L versus $211.6\pm78.8\times10^9$/L; P=.02). A 4-item symptom score based on the presence of cough before or concomitant with fever, myalgia, diarrhea, and rhinorrhea or sore throat detects SARS with 100% sensitivity and 75.9% specificity; a 6-item clinical score based on lymphopenia ($<1.0\times10^9$/L), thrombocytopenia ($<150\times10^9$/L) and the 4 symptom items detects SARS with 100% sensitivity and 86.3% specificity.

Conclusion: Certain symptoms and laboratory tests indicate higher risk of febrile probable SARS. In nonendemic areas, the febrile patients with recent contact with SARS or travel history to endemic areas could be screened for the probability of SARS by the use of clinical and symptom scores.

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Capsule Summary

What is already known on this topic

No rapid tests currently exist to distinguish severe acute respiratory syndrome (SARS) from common minor respiratory ailments in the emergency department (ED) setting.

What question this study addressed

Clinical features of 70 suspected SARS cases were studied to develop a scoring system to assist with rapid diagnosis of SARS in the ED.

What this study adds to our knowledge

A scoring system based on the presence of cough before or concomitant with fever, myalgia, diarrhea, rhinorrhea/sore throat, lymphopenia, and thrombocytopenia was helpful in discriminating cases that ultimately met the Centers for Disease Control and Prevention definition of probable SARS.

How this might change clinical practice

This scoring system has not been validated in other patient groups, and the diagnosis of SARS was not based on serology or polymerase chain reaction testing, but this is an important first step in developing diagnostic strategies for this new illness.

INTRODUCTION

Severe acute respiratory syndrome (SARS) has become a worldwide threat during a short period. Since the report of the first SARS case in Taiwan on March 15, 2003, hospital emergency departments (EDs) were soon inundated with patients who came back from affected areas[1] or those who had had close contact with them and wanted to rule out the possibility of having contracted SARS.[2] Identifying patients with a high probability of having SARS became imperative and needed to be done by using simple clinical characteristics. A scoring system is proposed according to our first experience of 70 febrile patients and will be used for future screening of suspected SARS cases.

MATERIALS AND METHODS

We undertook a prospective cohort study at the ED of National Taiwan University Hospital, a 2,400-bed tertiary university teaching hospital in northern Taiwan. From March 15, 2003, to April 2, 2003, we enrolled all patients presenting to the ED with a documented temperature higher than 38.0°C (>100.3°F), at home or at the ED, and with risk of exposure to SARS infection 14 days before onset of fever, irrespective of the presence of airway symptoms.

Since the outbreak of SARS, all febrile patients were evaluated in a designated area within the ED. All patients were assessed by emergency physicians using a structured SARS recording form developed a priori by the principal investigators, which includes the following items: detailed medical history, presenting symptoms, essential laboratory tests, and chest radiography results.[3] Other examinations were arranged according to clinical judgment by individual emergency physicians.

Admission was indicated for patients with any of the following: abnormal chest radiograph result, definite close contact history,[2] abnormal laboratory data, or impossible home quarantine (such as foreign traveler from affected area).

The admitted patients were followed up by contacting treating physicians and medical record review. The initially discharged patients were followed up by scheduled outpatient-clinic and telephone interview. All patients were followed up for at least 10 days after initial presentation.

The final diagnosis of probable case of SARS was based on Centers for Disease Control and Prevention criteria on April 10, 2003.[2] All patients not meeting such criteria were defined as non-SARS from clinical grounds.

Candidate items for the scoring system were selected from the SARS evaluation form and included symptoms, signs, and their sequence and laboratory test results. Items showing at least marginally significant differences between probable and non-SARS patients were then used to develop the scoring system.

Data were entered, processed, and analyzed with SPSS for Windows (release 10.0; SPSS, Inc., Chicago, IL). Binomial variables were analyzed with the Fisher-Freeman-Halton exact test. The Student's *t* test was used for comparisons of continuous variables of the 2 groups. All tests were 2-tailed. A *P* value of less than .05 was accepted as significant.

RESULTS

From March 15 to April 2, 2003, 224 patients with SARS exposure risks presented to our ED for ruling out the disease. Among the 224 patients, 72 had documented fever, at home or at the hospital, greater than 38°C (>100.3°F). Two of these 72 patients were lost to follow-up and were excluded.

There were 44 male patients and 26 female patients. The mean age was 42.8 years, ranging from 2 to 66 years.

Thirteen patients were admitted after ED evaluation. Eight patients were diagnosed as probably having SARS, all from the admitted group. The final discharge diagnosis for the remaining 5 patients for whom SARS was ruled out included mycoplasma pneumonia (1 case), legionellosis (1 case), bacterial bronchopneumonia (1 case), and nonspecific upper airway infections (2 cases).

Chest radiograph results were negative among all discharged patients. Chest radiograph results were positive in 9 of the 13 initially admitted patients. Among 9 admitted patients with positive radiograph results, 6 were diagnosed as probably having SARS; among 4 admitted patients with negative radiograph results, 2 were later diagnosed as probably having SARS. Among the 57 patients initially discharged from the ED, 40 patients were diagnosed with suspected cases of SARS before discharge, according to the World Health Organization case definition.[2] None of the 57 patients or their relatives developed SARS.

The initial clinical presentations of patients from both groups are summarized in Table 1. Compared with the non-SARS group, the SARS group has a significantly higher percentage of fever prolonged more than 5 days (87.5% versus 6.5%; $P<.01$), myalgia (75% versus 27.4%; $P=.01$), and diarrhea (50% versus 9.7%; $P=.02$) and less occurrence of cough before or concomitant with fever (0% versus 64.5%; $P=.01$).

Among the initial laboratory tests (Table 1), the SARS group had a significantly lower absolute lymphocyte count ($0.9\pm0.3\times10^9$/L versus $1.5\pm1.1\times10^9$/L; $P<.01$) and platelet count ($144.1\pm36.3\times10^9$/L versus $211.6\pm78.8\times10^9$/L; $P=.02$).

From univariate analysis, 6 clinical characteristics, including cough before or during fever, myalgia, diarrhea, fever longer than 5 days, lymphopenia ($<1.0\times10^9$/L), and thrombocytopenia ($<150\times10^9$/L) were significantly different between SARS and non-SARS groups. These characteristics became the basis for developing the clin-

Table 1.
Demographic data and initial presentation of febrile patients with risk of SARS.

	Non-SARS (N=62)		SARS (N=8)		
Final Diagnosis	**Mean±SD or No. (%)**	**95% CI**	**Mean±SD or No. (%)**	**95% CI**	***P* Value**
Age, y	44.0±9.8	37.2–50.8	33.9±15.9	29.9–37.8	.02
Sex, male/female	40/22 (64.5)	52.6–76.4	4/4 (50)	15.4–84.6	.46
Risk*					
Contact history	16 (25.8)	14.9–36.7	3 (37.5)	4.0–71.0	.48
Travel history	46 (74.2)	63.3–85.1	5 (62.5)	29.0–96.0	.48
Symptoms					
Cough†	40 (64.5)	52.6–76.4	0	0	.01
Rhinorrhea or sore throat	34 (54.8)	42.4–67.2	1 (12.5)	0–35.4	.06
Myalgias	17 (27.4)	16.3–38.5	6 (75)	45.0–100	.01
Headache	6 (9.68)	2.3–17.0	3 (37.5)	4.0–71.0	.06
Diarrhea	6 (9.68)	2.3–17.0	4 (50)	15.4–84.6	.02
Fever >5 d	4 (6.45)	0.3–12.6	6 (75)	45.0–100	<.01
Days from fever to ED, mean±SD	2.1±3.4	1.3–3.0	6.4±3.3	4.1–8.6	.001
Signs					
Fever at ED	19 (30.7)	19.2–42.2	3 (37.5)	4.0–71.0	.69
Temperature, °C	37.3±0.9	37.1–37.6	37.7±1.0	37.0–38.4	.36
Mean blood pressure, mm Hg	100.2±16.2	95.7–104.7	97±10	90.1–103.9	.60
Pulse rate, beats/min	100±19.8	94.6–105.4	103±13	94.0–112.0	.73
Oxygen saturation on room air, %	98.0±1.6	97.5–98.4	97.8±1.5	96.8–98.8	.71
Laboratory data					
WBC count ($\times10^9$/L)	8.6±3.7 (N=59)‡	7.7–9.5	6.1±5.1 (N=8)‡	2.6–9.6	.08
Hemoglobulin, g/dL	13.4±2.6 (N=59)‡	12.7–14.0	13.7±1.6 (N=8)‡	12.6–14.8	.75
Platelet count ($\times10^9$/L)	211.6±78.8 (N=59)‡	191.5–231.7	144.1±36.3 (N=8)‡	118.9–169.3	.02
Lymphocyte count ($\times10^9$/L)	1.5±1.1 (N=59)‡	1.2–1.8	0.9±0.3 (N=8)‡	0.7–1.1	<.01
Absolute neutrophil count ($\times10^9$/L)	6.2±3.3 (N=59)‡	5.4–7.0	4.8±5.2 (N=8)‡	1.2–8.4	.30
C-reactive protein, mg/dL	2.2±2.7 (N=35)‡	1.3–3.1	3.4±2.1 (N=7)‡	1.9–4.9	.28
Initial abnormal chest radiograph result	3 (4.8)	0–10.1	6 (75)	45.0–100	<.01

*The definition of risk: see text for details.
†"Cough" means that its occurrence was before or concomitant with fever.
‡N means numbers of patients with blood sampling initially.

ical decision rules. Because a positive chest radiograph result is one of the essential criteria for diagnosing probable SARS, it is not included in the prediction model. Rhinorrhea or sore throat was added because it exhibited borderline significance (P=.06).

Two sets of clinical decision rules were developed. For the 6-item clinical score (Table 2), with a cutoff value of 1, the sensitivity was 100% (95% confidence interval [CI] 0.68 to 1.0) and the specificity was 86.3% (95% CI 0.74 to 0.93) for detecting probable SARS. For the 4-item symptom score (Table 2), with a cutoff value of 0, the sensitivity was 100% (95% CI 0.68 to 1.0) and the specificity was 75.9% (95% CI 0.63 to 0.85) for detecting probable SARS.

DISCUSSION

In an endemic area of SARS, most reported cases had definite contact history with infected patients.[4] However, in nonendemic areas, patients presenting with fever and travel history to an endemic area create a challenge to emergency physicians. On one hand, overdiagnosis and stringent isolation of these patients could paralyze local health care facilities, but on the other hand, release of patients with possible SARS back to the community endangers the whole community. Development of clinical decision rules by using simple and readily available clinical characteristics for diagnosing probable SARS is therefore a public health priority.

Ho[5] suggests a management flowchart based on contact status. For the febrile and symptomatic patients without definite contact, if the chest radiograph result is normal, the flowchart suggests home charting of temperature and reassessment in 2 days. However, our experience suggests that travelers returning from endemic areas, even without chest radiograph findings on initial presentation, could turn out to be SARS positive; these individuals would be discharged improperly and continue to spread the disease in the community. By integrating clinical and laboratory characteristics, we proposed 2 sets of clinical decision rules that would be easily applicable in many settings in endemic and nonendemic areas.

In univariate analysis, clinical risk factors for SARS included younger age, myalgia, diarrhea, cough after the development of fever, and fever prolonged more than 5 days. In a case series in Hong Kong and Canada, reported cough was meaningful for SARS symptoms.[4,6,7] However, in our observation, only cough developed after fever is relevant to SARS. Laboratory risk factors included lymphopenia and thrombocytopenia.

According to the 6-item clinical score and the cutoff value of 1, patients presenting with a total score equal to or more than 1 would be considered as probably having SARS. If the scores are applied in clinics and EDs, the consequence of unnecessary admission and isolation could be minimized.

To make the screening process more applicable in settings in which laboratory data were not immediately available, such as the airport, the 4-item symptom score was developed. The score would be invaluable in screening a large number of possible patients, such as passengers in an airport.

There are several limitations in our study. First, the predictive ability of clinical and symptom scores needs to be validated in endemic and nonendemic areas. A validation study is currently under way in Taiwan. Second, the predictive ability could also be affected by the incidence of other infectious disease at the time. Third, until now the diagnosis of SARS was based mainly on clinical grounds.[2] The SARS status of our cohort could be altered when newer serologic or microbiologic tests become available. Finally, score systems based on reported symptoms are subject to recall bias. However, we believe our training of interviewers and the use of a structured questionnaire would minimize such concerns.

In the face of the emergence of worldwide SARS epidemics and the threats to the public health infrastructure, clinical decision rules using easily available clinical and laboratory characteristics are necessary for screening processes in health care facilities and nonclinical settings. We proposed 2 clinical decision rules

Table 2.
SARS score.[*]

Items	Initial Symptoms and Laboratory Findings	Score
A	Myalgias	1
B	Diarrhea	1
C	Cough[†]	–2
D	Rhinorrhea or sore throat	–1
E	Lymphopenia[‡]	1
F	Thrombocytopenia[§]	1

[*]Clinical score=A + B + C + D + E + F. If the total scores are zero or negative, then SARS is less likely. Symptom score= A + B + C + D. If the total scores are negative, then SARS is less likely.
[†]"Cough" means that its occurrence was before or concomitant with fever.
[‡]Lymphopenia is definited as lymphocyte count <1.0×10^9/L.
[§]Thrombocytopenia is definited as platelet count <150×10^9/L.

that could help identify SARS cases early and reduce unnecessary hospitalizations and isolations.

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Author contributions: SYC, CPS, WCC, and CYH conceived and designed the studies, collected data, and followed up all the enrolled patients. The trial was supervised and conducted by FYS, CLS, and SCC. CIK, KCT, and ZSY analyzed the statistic data and MHMM gave us statistic consultation. The manuscript was prepared by SYC, CPS, WCC, and CYH, and then revised by CIK and MHMM. SYC and WJC take responsibility for the paper as a whole.

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